# CASE REPORTS



## Constricting Exercises to Correct Postoperative Fecal Incontinence

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SOME degree of fecal incontinence is a distressing occasional aftermath of operations that involve the cutting of the sphincter ani, and operations performed with the intent of curing it may be unsuccessful.

The following report illustrates a method of treatment which enabled a patient so afflicted to regain complete control.

The patient, a young woman, had been operated upon for perirectal infection. Fecal incontinence had ensued, and another operation had not relieved it. Consequently, restraining opiates had been given and the patient was taking them when examined by the author.

Three fingers could be readily introduced into the anal canal. Upon them the patient could exert a feeble circular pressure. She was told that some of the circular fibres of the sphincter were still intact and that, just as a prizefighter could train and strengthen his hitting muscles by hitting exercises, so she could train and strengthen these fibres by constricting exercises.

The largest of a set of Young's anal canal dilators was introduced. This the patient could just retain. She was given the dilator and instructed she should, while lying down, introduce it several times a day, and each time try intermittently for a few minutes to grip it. She was informed she would soon be able to do this, and that then she would be given a smaller dilator and so on gradually until she could grip one of the smallest diameter. The patient followed the procedure conscientiously and in a few weeks reported that she had regained control except when walking.

Directed to stand up, to put her heels together, to separate widely the toe regions, and then to contract her buttock muscles, she at once felt the added protection. She was advised to walk with the feet thus splayed and while walking to practice the constricting exercises. In a few weeks the incontinence was completely corrected.

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## Erythermalgia

### Report of a Case, and Response to a New Therapeutic Approach

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SINCE the original report of erythermalgia by Weir-Mitchell in 1872[16] and his subsequent suggestion in 1878[17] that it be named "erythromelalgia," little was done in attempting to discover a rational method of therapeusis till the latter 1930s. In 1937 Mufson[18] suggested that the pronounced vasodilatation seen in this disease might be due to a lack of vasoconstrictor stimuli, and advised the use of epinephrine hydrochloride, either by inhalation or hypodermic administration. This was soon followed by Smith's and Allen's report in 1938[19] in which they recommended that the term "erythermalgia" be substituted for the original name suggested by Weir-Mitchell, and advocated the use of acetylsalicylic acid. They reported pronounced relief from the use of 0.65 gm. four or five times daily, the relief from a single dose sometimes lasting several days. Although no adequate explanation existed for this, as acetylsalicylic acid, except for its analgesic effects, pharmacologically at least, tended toward a greater cutaneous vasodilatation, Allen, Barker and Hines[2] came to regard this phenomenon as almost diagnostic of this disease process. In the light of more recent knowledge, the explanation of this may lie in the fact that salicylates in toxic doses are strong inhibitors of the enzyme hyaluronidase.[20] Although hyaluronic acid is not present in the capillary wall itself,[6, 15] it is known to make up the intercellular cement substance of the supporting connective tissue of these small vessels, and it is because of the weakening of this connective tissue cement substance that capillary damage occurs.[6] Possibly patients with erythermalgia may be more susceptible to this action of acetylsalicylic acid so that only small doses may be necessary to abolish the action of hyaluronidase and thus prevent the extravascular edema with the consequent distressing soft-tissue swelling. Despite the foregoing, however, Wright[22] has stated that in his experience acetylsalicylic acid gives patients only temporary relief and that the results of the administration of epinephrine by either route are far from striking.

Following the lead of Mufson,[18] whose concept of the physiopathology in this disease process seemed to be capable of explaining all the symptoms, it was decided to use a probable adrenalin precursor, which could be taken orally, for the purpose of producing a humoral antihistaminic vasoconstriction. For this purpose the amino acid l(—)-tyrosine together with its co-enzyme precursor, pyridoxine hydrochloride, was chosen as the form of therapy for a patient afflicted with erythermalgia. As there is evidence that tyramine, the amine derived from the amino acid tyrosine, may be identical with sympathin,[7] the rationale for its use seemed even more justified.

#### CASE REPORT

A white married woman, 30 years of age, was referred for study and treatment on account of a vasodilating type of peripheral vascular disease process, which had been diagnosed as erythermalgia and which she had been aware of since July 1947. The patient said that at that time, for no known reason, she first experienced a hot, and at times burning, throbbing pain in the fingers and toes, which was associated with swelling and reddening of the affected areas. This always followed either exposure of the extremities to heat (hot dishwater) or increased activity of the affected digits (knitting, etc.) and was relieved by immersing the parts in cold water. The swelling and redness would persist for hours after the disappearance of pain, so that the fingers of both hands generally appeared turgid. Because of this she had begun to shun social gatherings, as she was ashamed of the appearance of her hands. The upper extremities had always been much more affected than the lower, and the right upper extremity more than the left. On further questioning she admitted noticing an increasing intolerance to

heat during the previous 12 months, so much so that she at times felt as if she could not get her breath, and would have to open the windows to get relief. Three weeks previously a similar burning pain had developed in the left shoulder. She had attempted to relieve this with hot applications, only to discover that heat made it unbearable. The patient denied numbness, tingling, coldness, blanching or cyanosis of the affected digits, and stated that she knew of no family history of this disease. Prior to mid-1947 she had lived in New York where she had had no difficulty.

The patient stated that she had always been in good health until 1944, when she had had an appendectomy and the removal of cysts from the uterus and one ovary (presumably the right). Since then she had only had occasional attacks of frontal sinusitis which were always promptly controlled with penicillin inhalations. In January 1948 moderately severe left pyelonephritis had developed but it had responded well to penicillin. Menstrual periods had begun at the age of eleven, had always been regular, and the flow had always been moderate in character and duration. However, she had always been troubled with premenstrual cramps, which at times were severe enough to cause her to go to bed.

The family history was non-contributory. As for her habits, she generally smoked about ten cigarettes daily, used no alcohol as it made her hands swell. She denied using any drugs.

The patient had been examined and treated by the referring physician. Examinations done in March 1948 revealed erythematous, hot, swollen fingers and toes, a condition which could be brought on by immersing the extremities in hot water. An electrocardiogram showed no abnormality. The basal metabolic rate was —11. The blood cell count was within normal limits except for a relative eosinophilia (7 per cent), and the sedimentation rate was 4 mm. in one hour. Urine was normal. X-ray films of the chest, fingers and toes showed no evidence of disease in the lungs, bones or joints. Results of a cephalin flocculation test were negative. During the subsequent months the patient was treated with acetylsalicylic acid, then with propadrine hydrochloride orally, and finally with estrogen therapy parenterally, all without significant relief. She stated that she was unable to tolerate acetylsalicylic acid or propadrine hydrochloride, as the former caused gastric irritation and nausea, while the latter, in addition, was associated with considerable nervousness.

The patient was well-developed, alert and cooperative. The height was 67 inches and the weight 146½ pounds. The vessels in the fundus of the right eye were engorged, particularly the veins, but otherwise the eyegrounds were normal and there was no evidence of other abnormality in the head, neck, eye, ear, nose or throat. Except for occasional inspiratory rhonchi throughout both lower lung fields posteriorly, and a well-healed mid-rectus, lower abdominal scar, nothing of significance was discovered as regards the trunk, or thoracic, abdominal or pelvic organs. The blood pressure was 116 mm. of mercury systolic and 70 mm. diastolic on both sides.

All the fingers were erythematous, swollen to the point of being turgid, and warm. This was also true of the toes, but in them the surface temperature was somewhat lower. Peripheral arterial pulsations were present throughout and of excellent amplitude. Results of elevation-dependency tests were normal as regards return of color and venous filling time. Prolonged dependency led to the appearance of a mild cyanotic hue in all the toes. Skin temperatures and measurements of the circumference of various areas of the extremities appear in Table 1.

Therapy was instituted on January 17, 1949, 600 mg. of l(—)-tyrosine being given simultaneously with 24 mg. of pyridoxine hydrochloride* orally five times daily. The patient was told to return in one week. At the end of that time interval, she stated that four days after starting on this treatment she noticed a tingling sensation in the lower legs and feet and the lower arms and hands, on exposing the extremities to heat. The throbbing pain had disappeared as well as the swelling, but the hands and feet were now so cold that she had to warm them by artificial means. She could relieve the tingling by moving the affected parts of the involved extremities. Examination at this time revealed definite coldness of the hands and feet and wrinkling of the superficial skin of the fingers and toes. Because of what was interpreted as an overdosage, the medicinal compounds were decreased to l(—)-tyrosine 400 mg., and pyridoxine hydrochloride 16 mg. four times daily—before each meal and at bedtime. Care was taken not to administer ferrous salts, which have been shown to strongly inhibit the irritability of the musculature of the blood vessels to vasodilating and vasoconstricting agents.[13]

Since then the patient has continued on this dosage and has no recurrence of the symptoms associated with the distressing vasodilatation in the digits or of those connected with increased intolerance to heat. During the first week in February pain and tenderness in the right costovertebral angle developed in association with frequency and urgency of urination. Analysis showed the urine to be normal. The condition responded quickly to therapy with penicillin, sulfa drugs and tincture of hyoscyamus. An intravenous pyelogram

*l(—)-tyrosine and pyridoxine hydrochloride tablets used in this study were donated by Organic Chemicals, Inc., Pasadena, California.

TABLE 1.—*Measurements of Circumferences of Extremities and Readings of Temperatures at Various Times during Course of Treatment.*

| | MEASUREMENTS (CENTIMETERS) | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| | Date | | | | | | | |
| | 1-17-49 | | 1-24-49 | | 2-25-49 | | 3-16-49 | |
| Area | Rt. | Lt. | Rt. | Lt. | Rt. | Lt. | Rt. | Lt. |
| Thumb, proximal phalanx | 6.7 | 6.6 | 6.3 | 6.1 | 6.3 | 6.2 | 6.4 | 6.2 |
| Metacarpus | 20.2 | 19.6 | 19.8 | 19.2 | 19.9 | 19.2 | 20.0 | 19.3 |
| Wrist | 15.7 | 15.5 | 15.6 | 15.6 | 15.6 | 15.7 | 15.8 | 15.6 |
| First toe, proximal phalanx | 8.2 | 8.2 | 7.6 | 7.8 | 7.5 | 7.8 | 7.5 | 7.9 |
| Metatarsus | 24.4 | 24.8 | 24.0 | 24.0 | 24.2 | 24.0 | 24.0 | 24.1 |
| Ankle | 22.4 | 22.5 | 22.4 | 22.4 | 22.4 | 22.6 | 22.5 | 22.5 |
| Calf | 33.3 | 33.5 | 33.2 | 33.6 | 33.4 | 33.6 | 33.2 | 33.4 |
| | TEMPERATURES (CENTIGRADE) | | | | | | | |
| Room Temp. | 24.4 | | 24.0 | | 24.0 | | 24.4 | |
| Forehead | 34.5 | | 33.8 | | 34.2 | | 34.0 | |
| Index finger | 33.2 | 33.0 | 29.4 | 29.0 | 33.4 | 33.2 | 33.4 | 33.4 |
| First toe | 25.6 | 25.4 | 23.8 | 24.0 | 25.8 | 25.6 | 25.8 | 25.4 |
| Forefoot | 28.0 | 28.4 | 26.6 | 26.4 | 28.2 | 28.6 | 28.5 | 28.4 |

done on February 3, 1949, revealed a ptotic right kidney with a double pelvis, and what was interpreted as a probable aberrant vessel or kink at the right pelvic-ureteral junction without evidence of back-pressure. No calculi were noted along the urinary tract. It is of interest that since the start of the therapy the patient has had no premenstrual cramps. Skin temperatures and measurements of the extremities taken at random during the period of treatment appear in Table 1.

## DISCUSSION

Several of the natural indispensable amino acids are known precursors of humoral vascular stimulators. For example, the amino acid *histidine* is known to give rise to its amine, *histamine*, through the decarboxylation of its side-chain, and possibly by further chemical interactions to other histamine-like substances. In direct opposition to the latter, the amino acid *tyrosine*, which when decarboxylated produces the amine *tyramine*, is known by virtue of this last compound to produce an adrenalin-like effect.[12] Tyrosine however, unlike histidine, is not considered by most authorities to be an indispensable amino acid in view of the fact that it is thought to be a derivative of the essential amino acid *phenylalanine*.

In 1944 Bellamy and Gunsalus[5] demonstrated that the organism Streptococcus fecalis through its enzyme *tyrosine decarboxylase* was capable of decarboxylating the amino acid l(—)-tyrosine to its amine, *tyramine*. In the same year they announced that such decarboxylation required a co-enzyme which was a phosphorylated derivative of pyridoxine.[10] Such bacterial conversion, however, has been shown not to occur in the human intestine, as the pH of optimum activity for the bacterial enzyme, tyrosine decarboxylase, has been found to lie between 5 and 5.5.[8] As expressed by Hanke and Koessler,[11] the conversion of amino acids into their respective amines by bacteria "seems to be a protective mechanism which is resorted to when the accumulation of H ions within the organism's protoplasm is incompatible with its normal life processes." Gale and Epps[9] have further shown that in the definitely alkaline medium of the intestinal contents an alteration in the enzymic constitution of the bacterial cell takes place, and the bacterial reaction proceeds in an opposite way, the amino acid being deaminated to its keto acid in an effort to shift the reaction of the medium toward neutrality.

The evidence just stated rules out any production of the amine in question by intestinal bacteria. Such a reaction would then have to depend on the presence of a tissue enzyme. That such an enzyme exists was first shown by Holtz in 1937[12] and confirmed in the same year by Werle and Mennicken[21] working independently.

Thus the foregoing, in conjunction with the reactions to the administered compounds in the case reported, bears out the contention that the amino acid l(—)-tyrosine is capable of being transformed into a humoral adrenalin-like substance with vasoconstrictor properties, when combined with the tyrosine-decarboxylase co-enzyme precursor *pyridoxine hydrochloride*. Previous trials with l(—)-tyrosine alone or pyridoxine hydrochloride alone, by the author in other disease entities in which an over-histamine release is believed to be present, have been to no avail.

The response to therapy in the case here reported presents interesting physiological and physiopathological questions. It is to be noted that following the onset of therapy the patient complained of tingling in the extremities on exposure to heat, or on increased muscular activity. These are distinctly opposite to the original complaints of hot, burning, throbbing pains in fingers and toes when these were subjected to higher temperatures or the use of the parts was increased. As Anrep and his co-workers[3, 4] have shown that muscular contraction leads to a release of histamine, the patient's symptoms following an overdosage of l(—)-tyrosine and pyridoxine hydrochloride can only be interpreted as an over-adrenalin-like action relieved by the histamine release brought about by increased muscular contraction.

Of interest also is the fact that despite the continued decrease in the circumference of the affected parts, the skin temperature, except during the immediate period following the time of overdosage, has remained unchanged (see Table 1). This, then, would tend to indicate that the pathological process was one involving the deeper structures, that is, the hypodermis and the underlying muscular tissue, primarily, and the superficial skin layer only secondarily. In support of this contention lies the fact that despite the return of the skin temperatures to the pre-treatment level following a reduction in dosage, the edema of the affected parts did not reappear. In this connection it should be noted that the circumference measurements seem to bear out that the swelling in the disease-process involves the more distal parts only of each affected extremity, that is, the digits and possibly the metacarpal and metatarsal areas.

That histamine, besides being a potent vasodilator, is a strong contractor of uterine muscle is a well-established fact. The observation of the disappearance of premenstrual cramps which had been constantly present in the patient for many years, coupled with the cessation of the increased intolerance to heat and the symptoms of the vasodilating disease process, raises the question of an over-histamine release process in the patient, starting many years ago, but first showing itself in the form of cyclic premenstrual muscle spasms. Should further studies prove this to be true, then the disease erythermalgia could be looked upon as a gradually increasing overhistamine production throughout a period of many years, until the point of actual production of subjective and objective symptoms is reached. This, then, might provide an explanation for the distressing intermittent cramps experienced by some women prior to each menstrual cycle. For these might well be a reflection of an excessive histamine action, evidencing itself through the known oxytocic action of this organic constituent. In support of this contention is the finding by numerous investigators, and culminated by the work of Ahlmark,[1] that during pregnancy, when uterine contractions must be at a minimum, the histaminolytic power of the blood increases approximately 600-fold, and that of the placenta approximately 18,000-fold.

Because of these interesting aspects of the problem, further study is at present being carried on in related processes thought to be connected with a similar increased vasodilating-agent production, namely, hypotension, hypoglycemia, true allergic asthma, and other related allergic states.

## SUMMARY

A case of erythermalgia in a young woman is described.

The response of the disease to a new form of therapy consisting of the amino acid l(—)-tyrosine and pyridoxine hydrochloride is related.

The possibility of an over-histamine action as the basic cause in this disease entity is expressed, and theoretical considerations of the physiological and physiopathological aspects of the disease are commented on.

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## Intermittent Hydrarthrosis—Two Cases

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REVIEW of the American literature since 1941 reveals no reported cases of intermittent hydrarthrosis, a condition which was first reported by Perrin[8] in 1845, and apparently again by the same author in 1878. Relatively few cases have been reported since then, apparently only 120 in all. Two additional cases are reported herein, in the hope that interest will be stimulated with improvement in treatment.

Two varieties of intermittent hydrarthrosis have been encountered and reported: (1) symptomatic intermittent hydrarthrosis, and (2) idiopathic intermittent hydrarthrosis. In the first classification the recurrent joint swellings are harbingers of typical rheumatoid arthritis. Idiopathic intermittent hydrarthrosis usually occurs in persons who have recurrent attacks without the development of rheumatoid disease later.

### ETIOLOGY

The cause of this condition is apparently unknown, but it is worthy of note that all cases reported have been in the white race, that often the disease has occurred in persons with brucellosis (Sharpe[12] and Baker[1]) and that often it was of definite allergic origin (Lewin and Taub,[7] Berger,[2] Schlesinger,[10] Cook,[3] and Service[11]).

### SYMPTOMS

Any joint may be involved, but the condition has a predilection for the knee, which was the joint affected in the cases to be reported. In most cases the onset is in the third or fourth decades of life. The disease may be bilateral, but in a majority of the cases reported a single joint was involved. Onset is usually abrupt with moderate pain, definite joint swelling, and limitation of motion. There are usually no signs of local inflammation, regional adenopathy, or lymphatic involvement. Even mild febrile reaction is rare. After a variable period of time, which is usually specific for each individual, the joint effusion disappears, then reappears in from seven to 21 days. Local disability, with limitation of motion and occasional pain on pressure, is usual. The total duration of the cycles of this disease may be up to 20 plus years. Laboratory findings are extremely variable. Secondary anemia and an accelerated sedimentation rate may be present.

### DIFFERENTIAL DIAGNOSIS

Differential diagnosis is usually not too difficult, since complete examination of the patient can usually eliminate trauma, joint manifestations of systemic diseases (tuberculosis, gonorrhea, syphilis, or brucellosis), and reactions due to administration of antigens or vaccines. Radiographic examinations show a classical picture of severe hydrarthrosis without remarkable joint changes.

### PATHOLOGY

Authorities do not agree as to the exact changes to be expected. Ghormley and Deacon[4] reported slight thickening of the lining layer of cells without perivascular thickening or fibrosis. Schlesinger[10] stated that the knees are usually involved because they have an especially large arterial circulation, extraordinarily well supplied with medullated nerve fibers. Porter[9] and others have observed changes consistent with those of early rheumatoid arthritis. Examination of aspirated synovial fluid will often show 100 cells per cu. mm., with more than 50 per cent of the cells being polymorphonuclear leukocytes. Culture and experimental animal inoculations have not consistently shown growth or infection in any cases reported.

### TREATMENT

Salicylates have been used in full doses with no response. Older forms of therapy (quinine, arsenic, aspiration and lavage of the affected joints with the introduction of antiseptic solutions, desensitization, and peptone) have all been